# Nutritional management of Crohn's disease with a peptide-based enteral formula

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We examined a nutritional approach to the therapy of Crohn's disease with an enteral formula ('Enterued', Terumo Corporation, Tokyo, Japan) which contains low molecular weight peptides as a protein source.

Total protein, albumumin, transferrin, prealbumin and retinol-binding protein levels were significantly increased as indices of the nutritional status, when compared with those observed before treatment.

White blood cell count (WBC), erythrocyte sedimentation rate and C reactive protein (CRP) as the indices of inflammation levels were reduced significantly after the termination of the treatment, when compared with those observed before treatment.

The International Organization for the Study of Inflammatory Bowel Disease (IOIBD) assessment scores decreased in all cases, except for one case out of 51 cases evaluated.

Deterioration in nutritional status was not observed in any patient, but rather was maintained or improved; 42 out of the total 51 cases (82.4%) exhibited at least moderate improvement.

Treatment was discontinued on account of side effects such as abdominal distension, abdominal pain and diarrhoea in five cases (8.1%).

The enteral formula 'Enterued', utilizing low molecular weight peptides as a nitrogen source, appears to improve nutritional status and encourage remission of the inflammatory process with minimal side effects.

#### Introduction

Crohn's disease is a non-specific, recurrent, granulomatous, inflammatory bowel disease, with as yet unknown causes. The clinical features of the disease include a cobblestone appearance, longitudinal ulceration and fibrosis along the length of the digestive tract, from oesophagus to rectum, although it is most common in the lower part of the ileum. Consequently the patient may suffer from malabsorption and malnutrition which are difficult to treat.

At present, there is no established treatment strategy for Crohn's disease and in cases where remission is achieved, it is desirable to maintain this for as long as possible. There is no established means to achieve and maintain remission. Recently it has been reported that an elemental diet supplementation is effective during the acute stage and in maintenance of remission<sup>1-3</sup>.

Conventionally, crystalline amino acids, soya protein, milk protein, and casein have been amongst sources of nitrogen in enteral nutrition. However, in 1960 Newey et al.<sup>4</sup> reported the absorption of di- and tripeptides in the

small intestine later and Matthews et al.<sup>5</sup> and Adibi et al.<sup>6,7</sup> reported that low molecular weight peptides such as di- and tripeptides were absorbed more rapidly than amino acids. In 1980 Silk et al.<sup>8</sup> reported that low molecular weight peptides were observed in the portal vein after absorption in a form similar to the composition of the amino acids administered.

Now 'Enterued', an enteral feed containing low molecular weight peptides as a nitrogen source, is available to patients. We have undertaken a multicentre study of a nutritional therapy for Crohn's disease in Japan (Table 1) using 'Enterued'. We report its effect from both the nutritional and inflammatory points of view.

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Table 1. Summary of participating medical centres

1	Sapporo Medical College	Internal Medicine I
2	Asahikawa Medical College	Internal Medicine III
3	Hirosaki University, School of Medicine	Internal Medicine I
4	Akita University School of Medicine	Internal Medicine I
5	Iwate Medical University, School of Medicine	Internal Medicine I
6	Tohoku University, School of Medicine	Internal Medicine III
7	Yamagata University, School of Medicine	Internal Medicine II
8	Niigata University, School of Medicine	Internal Medicine III
9	Niigata Municipal Hospital	Gastroenterology
10	The University of Tsukuba, School of	
	Medicine	Internal Medicine
11	National Defense Medical College	Internal Medicine II
12	School of Medicine, Keio University	Internal Medicine
13	Nihon University, School of Medicine	Internal Medicine III
14	The Jikei University School of Medicine	Internal Medicine I
15	National Hospital Centre	Gastroenterology
16	Social Insurance Central Hospital	Internal Medicine
17	Shinshu University, School of Medicine	Internal Medicine II
18	Yokohama City University, School of	
	Medicine	Internal Medicine III
19	East Hospital, Kitasato University	Internal Medicine
20	School of Medicine, Tokai University	Internal Medicine VI
21	School of Medicine, Gifu University	Internal Medicine I
22	Medical School, Nagoya City University	Internal Medicine I
23	Aichi Cancer Centre	Gastroenterology
24	Shiga University of Medical Science	Internal Medicine II
25	Otsu Red Cross Hospital	Internal Medicine III
26	Kyoto Prefectural University of Medicine	Internal Medicine I
27	Kyoto Prefectural University of Medicine	Internal Medicine III
28	Osaka City University, Medical School	Internal Medicine III
29	Hyogo College of Medicine	Internal Medicine IV
30	Hiroshima University School of Medicine	Internal Medicine I
31	School of Medicine, Fukuoka University	Health Care Centre
32	Chikushi Hospital, School of Medicine,	
	Fukuoka University	Internal Medicine
33	School of Medicine, University of the	
_	Ryukyus	Internal Medicine I

#### Materials and methods

# 'Enterued' profile

'Enterued' is an enteral formula developed and supplied by Terumo Corporation (Tokyo, Japan). It is a source of protein containing a mixture of small peptides of an average molecular weight of 330. Over 70% of the peptides are di- and tripeptides derived from egg-white hydrolysate. Dextrin and a 1:1 mixture of soybean and corn oils constitute carbohydrate and fat sources respectively. The product also contains vitamins and electrolytes based on the Japanese recommended dietary intakes (Table 2). The osmolality is 530 mOsm/kg as a solution of 1 kcal/ml (4.18 kjoule/ml).

#### Protocol

#### Subjects

Patients with Crohn's disease aged 12 years or older were recruited for this study, except in instances where enteral nutrition was not possible/suitable, or where there were severe complications such as ileus, hepatic or renal failure.

Prior to the study informed consent was obtained, verbally, or in writing by the doctor, for each patient in relation to the purpose of the study, its expected efficacy and possible side effects.

#### Administration mode

'Enterued' was administered via a polyurethane nasogastric feeding tube into the stomach, using a pump to maintain a constant infusion rate. 'Enterued' (1 kcal/ml)

Table 2. Composition of Enterued®

	Per bag (100 g)	Solution of 1 kcal/ml
	, ,,	(4.18 kjoule/ml)
EWH (egg white hydrolysate)	18.4 g	
average molecular weight of 3	,	
Dextrin	72.0 g	
Fat (soybean oil:corn oil=1:1)	5.0 g	
Minerals		
Na	300 mg	( 32.6 mmol/l)
K	300 mg	( 19.2 mmol/l)
Cl	600 mg	( 42.3 mmol/l)
Ca	300 mg	( 18.7 mmol/l)
P	200 mg	( 16.1 mmol/l)
Mg	86 mg	( 8.8 mmol/l)
Fe	2.9 mg	(129.8 µmol/l)
Zn	1.5 mg	( 57.3 μmol/l)
Mn	0.6 mg	( 27.3 μmol/l)
Cu	0.2 mg	( 7.9 μmol/l)
Vitamins		
Retinol palmitate	1000 IU	
Thiamine hydrochloride	1.0 mg	
Riboflavin	1.0 mg	
Pyridoxine hydrochloride	1.0 mg	
Cyanocobalamine	2 μg ·	
Ascorbic acid	200 mg	
Chole-calciferol	100 IU	
Tocopherol acetate	30 IU	
Phytonadione	0.5 mg	
Nicotinamide	10 mg	
Calcium pantothenate	2.0 mg	
Folic acid	0.2 mg	
Biotin	50 μg	
Choline chloride	20 mg	
Inositol	20 mg	
Energy	400 kcal	
Nitrogen	2.34 g	

was infused initially at 40 ml/h, and then the dose was increased stepwise every two or three days, paying attention to the clinical condition, up to 100 to 150 ml/h for about seven days after the initiation of the treatment. Maintenance dose was 1200 to 2400 kcal/day (5016 to 10 1032 kjoule/day) depending on the patient's condition. The treatment period was two weeks to two months. During the treatment, the patients were nourished mainly by 'Enterued', which provided 70% or more of the total energy needed, even where food ingestion continued.

#### Examination items

Common case cards were kept for all patients, on which the condition, administration mode and various clinical parameters were recorded.

Haematological and biochemical serum investigations covered red blood cell count (RBC), white blood cell count (WBC), haematocrit, lymphocyte(%), haemoglobin, erythrocyte sedimentation rate, total protein, albumin, blood sugar, urea nitrogen, creatinine, total bilirubin, triglycerides, total cholesterol, glutamic-oxalacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), alkaline phosphatase (Al-P), gammaglutamyl transpeptidase (γ-GTP), sodium, potassium, chloride, calcium, phosphorus and C reactive protein (CRP). Some patients were examined for transferrin (Tf), prealbumin (PA), retinol-binding protein (RBP) and plasma aminogram.

These investigations were carried out three times: before, during (on day 14) and after the treatment.

#### Evaluation items

Patients were evaluated for degree of nutritional improvement, and overall safety and 'Therapeutic usefulness' was judged by the physician-in-charge.

Based on clinical condition and such indices of nutritional status as body weight, arm circumference and others derived from laboratory investigations, nutritional improvement was classified by the physician-in-charge into six degrees: (1) marked improvement; (2) moderate improvement; (3) mild improvement; (4) no change; (5) exacerbation; or (6) judgement impossible.

Based on the evaluation of nutritional improvement and overall safety, the physician-in-charge classified the 'therapeutic usefulness' into five degrees: (1) very useful; (2) substantially useful; (3) moderately useful; (4) no decision; and (5) no usefulness.

The International Organization for the study of Inflammatory Bowel Disease (IOIBD) assessment scores were determined on the basis of its report<sup>9</sup>.

#### **Statistics**

Student's t test was used on sequential data for statistical analyses.

Table 3. Clinical profile of subjects

	Small intestinal type	Large intestinal type	Small and large intestinal type	Total
Number of subjects	18 (2)	12 (2)	32 (7)	62 (11)
of analysis				
Sex				
Male	15 (2)	9 (2)	25 (5)	49 (9)
Female	3 (0)	9 (2)	7 (2)	13 (2)
Age				
15 or younger	0 (0	0 (0)	3 (0)	3 (0)
16 to 19	5 (0)	3 (0)	7 (1)	15 (1)
20 to 29	5 (1)	6 (2)	18 (6)	29 (9)
30 to 39	7(1)	2 (0)	3 (0)	12 (1)
40 to 49	1(0)	1 (0)	1 (0)	3 (0)
Body weight				
Under 40 kg	0 (0)	1(0)	2 (0)	3 (0)
40 to 50 kg	2(1)	6 (1)	14 (3)	22 (5)
50 to 60 kg	9(1)	2 (0)	12 (3)	23 (4)
Over 60 kg	6 (0)	3 (1)	4 (1)	13 (2)
Unknown	1 (0)	0 (0)	0 (0)	1(0)
Complication				
Yes	4(0)	3 (0)	1 (0)	8 (0)
No	14(2)	9 (2)	31 (7)	54 (11)
Nutritional condition				
Good	3 (0)	1(0)	4 (1)	8 (1)
Fair	9(1)	6 (1)	14 (4)	29 (6)
Poor	6 (1)	6 (1)	14 (4)	29 (6)

<sup>( ):</sup> Number of cases analysed only for overall safety

#### Results

Subject characteristics (Table 3)

A total of 63 cases were treated with 'Enterued'. One case, where another enteral nutrient was concomitantly used, was excluded from the analysis. The remaining 62 cases included 49 males and 13 females. The 62 cases subjected to analysis comprised cases of Crohn's disease

of the small intestine in 18, of the large intestine in 12, and of the small and large intestine type in 32. The ages ranged from 12 to 48 year, with the average being 24.7 years.

A total of 11 cases required analysis only for overall safety because: (1) the treatment periods were less than 14 days; (2) the average contributions of 'Enterued' to the total energy administered were less than 60%; or (3) the doses of 'Enterued' were less than 1200 kcal/day (5016 kJ/day).

There were eight cases where complications were observed prior to 'Enterued' administration and 11 cases where there had been surgery of the digestive tract previously.

Table 4. Administration mode

	Small intestinal type	Large intestinal type	Small and large intestinal type	Total
Number of subjects of analysis	18 (2)	12 (2)	32 (7)	62 (11)
Treatment period				
10 days or less	0 (0)	1(1)	5 (5)	6 (6)
11 to 20 days	3 (2)	1(0)	4 (1)	8 (3)
21 to 30 days	3 (0)	1(0)	7 (0)	11 (0)
31 to 40 days	4 (0)	2(0)	5 (0)	11 (0)
41 to 50 days	3 (0)	3 (1)	3 (0)	9 (1)
51 days or more	5 (0)	4 (0)	8 (1)	17 (1)
Administration site				
Stomach	8 (2)	6 (1)	16 (4)	30 (7)
Duodenum	5 (0)	1(0)	6 (1)	12 (1)
Jejunum	1(0)	3 (0)	9 (1)	13 (1)
Per os	4(0)	2 (1)	1 (1)	7 (2)

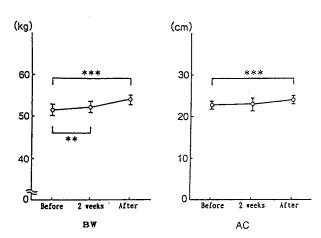
<sup>():</sup> Number of cases analysed only for overall safety

Enteral administration conditions (Table 4)

Treatment periods ranged from two days to 75 days, with the average being 37 days.

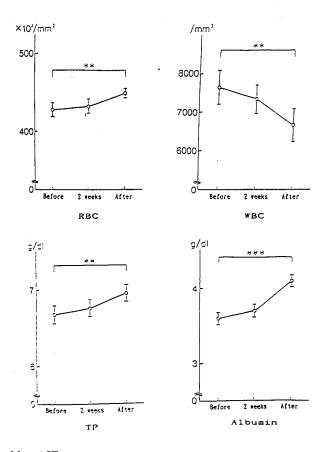
Maximum daily energy administered ranged from 800 to 3000 kcal (from 3344 to 12 540 kJ), with the average being 2136 kcal (8928 kJ).

The intubation tube was situation in the stomach in 30 cases, duodenum in 12 cases, jejunum in 13 cases and per os in seven cases.



\*\*: P<0.01 \*\*\*: P<0.001

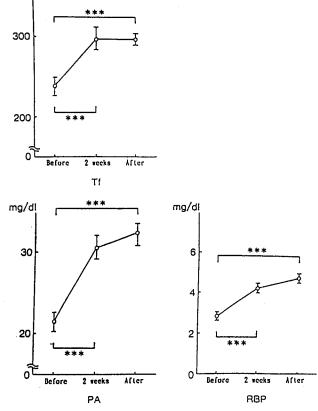
Fig. 1 Physical nutritional status (body weight [BW], arm circumference [AC]: values are means  $\pm$  SE.



Mean±SE \*\*:P<0.01 \*\*\*: P<0.001

mg/dl

Figure 2. Red Blood cell count (RBC), white blood cell count (WBC), haematocrit (TP) and albumin.



Mean±SE \*\*\*: P<0.001

Figure 3. Rapid turnover protein (transferrin [Tf], prealbumin [PA], retinol-binding protein [RBP]).

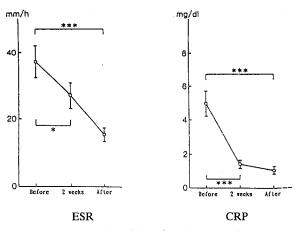


Figure 4. Inflammation index (erythrocyte sedimentation rate [ESR], C reactive protein [CRP]).

# Nutritional indices and laboratory investigations

Figures 1 to 4 show the results of physical nutritional status and of haematological and biochemical investigations of serum and special blood tests.

The results of the physical nutritional status indicated significantly increased body weight and arm circumference (AC) after two weeks or after the termination of the treatment, when compared with those observed before treatment (Fig. 1). The haematological indices revealed a significant increase in red blood cell count (RBC) and a significant decrease in white blood cell count (WBC) with treatment (Fig. 2). The results of the biochemical examination of serum indicated significantly increased total protein and albumin as indices of the nutritional status when compared with those observed before treatment (Fig. 2). Triglyceride and total cholesterol levels were also significantly higher (triglycerides:  $97.18\pm5.93 \text{ mg/dl [before] vs } 131.78\pm11.11 \text{ mg/dl [after]}$  $-\text{mean}\pm\text{SE}$ ; P<0.01, total cholesterol: 137.88 $\pm$ 5.22 mg/dl [before] vs 149.59±6.67 mg/dl [after]  $-mean\pm SE$ ; P<0.05). Significantly higher levels of transferrin, prealbumin and retinol-binding protein were observed after two weeks of the treatment. The tendency to increase was maintained even after the termination of the treatment (Fig. 3). The indices of inflammation, erythrocyte sedimentation rate and CRP were significantly lower after two weeks, as well as after the termination of the treatment, when compared with those observed before treatment (Fig. 4). Otherwise levels of blood sugar, urea nitrogen, creatinine, total bilirubin, GOT, GPT, Al-P, γ-GTP, sodium, potassium, chloride and aminogram

within normal values and remained unchanged.

#### IOIBD assessment scores

Except for one case out of 51 evaluated, all showed decreased scores. Eleven cases had scores of zero or one and maintained the scores. Thirty-one out of 40 cases, having scores of two or more, reduced their scores to zero or one. Other cases also exhibited a decrease in score.

Forty-two out of 51 cases (82.4%) exhibited scores of one or less after treatment.

In ten out of ten cases (100%) of the large intestine type, 14 out of 16 cases (87.5%) of the small intestine type and 18 out of 25 cases (72.0%) of the small and large intestine type, scores decreased to zero or one.

Figure 5 shows the results obtained with or without the

Table 5. Nutritional improvement evaluation\* (with or without concomitant drugs)

State of improvement i	Marked improvement	Moderate improvement	Mild improvement	No change	Exacer- bation	Total	Improvement rate§ (moderate or better)
Without concomitant d	rugs						
Type of disease							
Small intestinal type	2	5	1	1	0	3	77.8%
Large intestinal type	1	2	0	0	0	3	100.0%
Small and large intestinal type	6	3	2	0	0	11	81.8%
Total	9	10	3	1	0	23	82.6%
With concomitant drug Type of disease	s	* '					
Small intestinal type	6	0	1	0	0	7	85.7%
Large intestinal type		2	0	0	0	7	100.0%
Small and large intestinal type	2	8	2	2	0	14	71.4%
Total	13	10	3	2	0	28	82.1%

<sup>\* &#</sup>x27;Nutritional improvement' was assessed by a combination of observed clinical condition (bedside nutritional status) measurements of weight and arm circumference and laboratory investigations.

'Improvement rate' is defined by the ratio of number of cases exhibiting at least moderate improvement to total cases subjected to analysis.

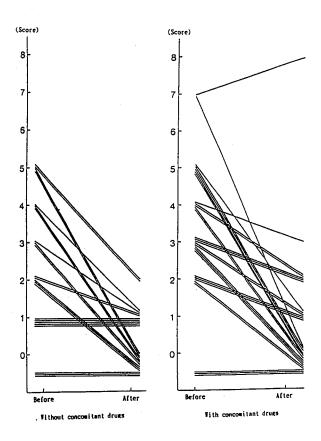


Figure 5. International Organization for the Study of Inflammatory Bowel Disease (IOIBD) assessment scores (with or without concomitant drugs).

concomitant use of salazopyrin or prednisolone.

Twenty-one out of 28 cases with concomitant drugs and 21 out of 23 cases without concomitant drugs exhibited scores of zero or one after enteral nutrition treatment. The tendency to decrease score was observed regardless of concomitant drug usage when classified by disease type.

#### Overall evaluation

Nutritional improvement. Deterioration in nutritional condition was not observed in any case; 42 out of the total 51 cases (82.4%) exhibited at least moderate nutritional improvement, including 13 out of 16 cases (81.3%) of the small intestine type, ten out of ten cases (100%) of the large intestine type and 19 out of 25 cases (76.0%) of combined small and large intestine type of Crohn's disease. When there was concomitant use of drugs and enteral nutrition, no significant difference between enteral nutrition alone was observed (Table 5).

Overall safety. Evaluation by the physician-in-charge of the 62 cases revealed that 'Enterued' was discontinued due to side effects in five cases (8.2%), mild side effects were observed in five cases (8.2%) and 'Enterued' was safely administered without side effects in 52 cases (83.9%).

Side-effects observed in the five cases in which 'Enterued' was discontinued included abdominal distension and abdominal pain, while in two of these cases side-effects could be attributed to the high concentration of the initial administration. In the five cases with mild side effects of similar kind, these disappeared and treatment was continued.

Overall therapeutic usefulness. Forty-two out of total 51 cases (82.4%) including 14 out of 16 cases (87.5%) of the small intestine type, ten out of ten cases (100%) of the large intestine type and 18 out of 25 cases (72.0%) of the small and large intestine type were judged to have benefited. When the concomitant drug usage was considered, no significant difference was observed (Table 6).

#### Discussion

The usefulness of the peptide formula 'Enterued' in Crohn's disease was examined at 33 centres in Japan.

Except for 11 cases where the treatment period using 'Enterued' was less than 14 days and the dose was less

Table 6. Therapeutic usefulness evaluation<sup>a</sup> (with or without concomitant drugs)

Usefulness	Very useful	Substantially useful	Moderate useful	No decision	No usefulness	Total	Usefulness rate <sup>b</sup> (substantially useful or better)
Without concomitant dr	ugs						
Type of disease	<i>-</i>						
Small intestinal type	4	4	0	0	1	9	88.9%
Large intestinal type	1	2	0	0	0	3	100.0%
Small and large	8	1	1	1	0	11	81.8%
intestinal type				-			
Total	13	7	1	1	1	23	87.0%
With concomitant drugs							
Type of disease							
Small intestinal type	4	2	1	0	0	7	85.7%
Large intestinal type	4	3	0	0	0	7	100.0%
Small and large	3	6	2	2	1	14	64.3%
intestinal type							
Total	11	11	3	2	1	28	78.6%

<sup>&</sup>quot;Therapeutic usefulness' was assessed by a combination of 'Nutritional improvement' (see Table 5) and of 'safety' judged by treatment period, proportion of energy intake achieved from 'Enterued', where total energy intake was less than 1200 kcal (5016 kJoules) per day and where side-effects probably occurred.

than 60% of total daily energy and less than 1200 kcal (5016 kJ), the nutritional indices after treatment in 51 cases showed significant increases in levels of rapid turnover proteins such as transferrin, prealbumin and retinol-binding protein. Significant increases were observed in albumin and total serum protein levels after the termination of the treatment, but not during. CRP also showed significant reduction after two weeks. This indicates that effective nutritional therapy with 'Enterued' is possible.

It must be acknowledged, however, that this was not a blind, controlled study group assessed against placebo, but rather a study of subjects before, during, and after treatment.

Body weight, circumference of triceps muscle of the upperarm, RBC, and levels of total protein, albumin, total cholesterol and tiyglycerides showed a significant increase after the termination of the treatment (average 42 days). Since the significant increases were observed in both biochemical nutritional indices and anthropometric indices, 'Enterued' may be considered useful at an early stage.

Significant reductions observed in erythrocyte sedimentation rate, CRP and WBC as inflammatory indices indicate an improvement in the inflammatory process.

Low IOIBD assessment scores achieved in most patients also indicate improvement in clinical condition.

One case of combined small and large intestinal Crohn's disease where the IOIBD assessment score increased after treatment may reflect a reduced fat absorption due to ileocecal resection.

Enteral nutrition treatment has been used not only for pre- and post-operative nutritional supplementation, but also for nutritional management of those patients with malabsorption syndromes. Especially in idiopathic inflammatory bowel diseases (such as Crohn's disease) it may offer a therapeutically effective and non-toxic alternative to conventional surgery and drugs<sup>10</sup>.

In Japan nutritional therapy using an elemental diet,

which contains a mixture of free L-amino acids as a nitrogen source, has also been considered as primary therapy for Crohn's disease<sup>11-13</sup>.

There have been few reports on the efficacy of defined formulae such as those containing peptides or protein in the management of acute Crohn's disease. Malchow et al. 14 showed the efficacy of treatment of active Crohn's disease with a peptide-containing formula compared with the combination of 6-methyl-prednisolone and salfusalazine. Gassull et al. 15 demonstrated a beneficial effect of enteral nutrition with a polymeric diet on the nutritional state of Crohn's disease, but an overall therapeutic effect could not be proved.

Hiwatashi<sup>16</sup> et al. have examined the therapeutic effect of the elemental diet 'Elental' (Ajinomoto Company, Tokyo, Japan) in 41 cases of Crohn's disease, and found improvement in 85% of them. In our study, 'Enterued' showed comparable results.

The usefulness of 'Elental' in Crohn's disease is considered to be due to the utilization of amino acids as a nitrogen source and to the extremely low fat content. On the other hand, 'Enterued' consists of small peptides and has a fat content of 5%. It is interesting that 'Enterued' exhibited a usefulness comparable to 'Elental'.

Peptides, 70% of which mainly contain di- and tripeptides, may have little antigenicity, while being absorbed more readily than amino acids<sup>5,6</sup>. A fat content of 5% is also advantageous since there is no need to infuse the fat emulsion intravenously to prevent essential fatty acid deficiency.

Although salazopyrin and prednisolone may be given in Crohn's disease as in the therapy of ulcerative colitis, the results of our study indicate an equivalent efficacy of 'Enterued' irrespective of concomitant drugs.

'Enterued' exhibited side-effects in ten out of 62 cases (16.1%), and there were only five cases (8.1%) where enteral feeding was discontinued due to side effects, such as abdominal pain or diarrhoea, two of which were probably due to a high concentration of the initial

b 'Usefulness rate' is defined by the ratio of number of cases exhibiting at least substantially useful to toal cases subjected to analysis.

infusion. Also, in five cases (8.1%) where mild side effects were observed, these gradually disappeared and treatement could be continued. These observations suggest that 'Enterued' can be administered safely.

#### References

- 1 O'Morain C, Segal AW, Levi AJ. Elemental diets in treatment of acute Crohn's disease. Br Med J 1980; 281:1173-5.
- 2 Morin CL, Roulet M, Roy CC, Weber A, Lapointe N. Continuous elemental enteral alimentation in the treatment of children and adolescent with Crohn's disease. J Parent Ent Nutr 1982; 6:194-9.
- 3 Saverymuttu S, Hodgson HJF, Chadwick VS. Controlled trial comparing prednisolone with an elemental diet plus non-absorbable antibiotics in active Crohn's disease. Gut 1985; 26:994–8.
- 4 Newey H, Smyth DH. Intracellular hydrolysis of dipeptides during intestinal absorption. J Physiol 1960; 152:367–80.
- 5 Craft IL, Geddes D, Hyde CW, Wise IJ, Matthews DM. Absorption and malabsorption of glycine and glycine peptides in man. Gut 1968; 9:425–37.
- 6 Adibi SA, Phillips E. Evidence for greater absorption of amino acids from peptide than from free form in human intestine. Clinical Research 1968; 16:446.
- 7 Adibi SA. Intestinal transport of dipeptides in man: relative importance of hydrolysis and intact absorption. J Clin Invest 1971; 50:2266-75.
- 8 Silk DBA, Fairclough PD, Clark ML, Hegarty JE, Marrs TC, Addison JM, Burston D, Clegg KM, Matthews DM. Use of a peptide rather than free amino acid nitrogen

- source in chemically defined 'elemental' diets. J Parent Ent Nutr 1980; 4:548–53.
- 9 Dombal FT, Softley A. IOIBD report nol:observer variation in calculating indices of severity and activity in Crohn's disease. Gut 1987; 28:474-81.
- 10 O'Morain C, Segal AW, Jevi AJ. Elemental diet as primary treatment of acute Crohn's disease:a controlled trial. Br Med J 1984; 23:1859-62.
- Hiwatashi N, Konno Y, Kobayashi K, Goto Y, Unoura A, Sato T, Endo K, Watanabe H, Matsumoto K, Mochizuki F. The therapeutic effectd of elemental diet in Crohn's disease. Gastroenterological Endoscopy (Japanese) 1982; 24:578–84.
- 12 Fukuda Y, Shimoyama T. Crohn's disease and hyperalimentation. The Japanese Journal of Parenteral and Enteral Nutrition (Japanese) 1991; 13:227–31.
- 13 Shoda R, Matsueda K, Yamato S, Takemasa Y, Unno J, Katsuta E, Tanaka A, Matsukawa M, Masaki N, Hayashi S, Shimojo E, Umeda N. Elemental enteral hyperalimentation in Crohn's disease: its therapeutic efficacy and limitations. Digestion & Absorption (Japanese) 1992; 15;102-5.
- 14 Malchow H, Steinhardt HJ, Lorenz-Meyer H, Strohm WD, Rasmussen S, Sommer H, Jarnum S, Brandes JW, Leonhardt H, Ewe K, Jesdinsky H. Feasibility effectiveness of a defined-formula diet regimen in treating active Crohn's disease. European Cooperative Crohn's Disease Study III. Scand J Gastroenterol 1990; 25:245–244.
- 15 Gassull MA, Abad A, Cabre E, Gonzalez-Huix F, Gine JJ, Dolz C. Enteral nutrition in inflammatory bowel disease. Gut 1986; 27:S1,76–80.
- 16 Hiwatashi N. Nutritional therapy for Crohn's disease. Current Therapy (Japanese) 1989; 7:229-33.

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#### 要旨

窒素源として低分子ペプチドを用いた経腸栄養剤(「エンテルード」テルモ社製)を用い、クローン病に対する栄養療法について検討した。栄養指標とした総蛋白、アルブミン、トランスフェリン、プレアルブミン及びレチノール結合蛋白は投与前に比べて有意に上昇した。白血球数(WBC)並びに炎症指標である血沈値、C反応性蛋白(CRP)は投与前に比べ投与終了後には有意に減少した。IOIBDスコアーは、1例を除き全ての症例で減少した。栄養状態が悪化した症例はなく、全51例中42例(82.4%)で中等度以上の改善を示し、また全ての症例で維持以上の効果が認められた。投与を中止した5症例の副作用は、腹部膨満感、腹痛、下痢などであった。

低分子ペプチドを窒素源とする経腸栄養剤「エンテルード」は、栄養改善効果及び炎症 の改善が優れており、副作用も少なく安全に投与できた。

# Nutritional management of Crohn's disease with a peptide-based enteral formula

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# 用小肽爲基礎的腸道管飼配方 對克羅恩氏病(CROHN'S DISEASE)的營養處理 摘要

我們檢驗了一種以低分子肽供給蛋白質的腸道管飼配方(ENTERUED, 日本,東京,TERUMO 公司生産)對克羅恩氏病(CROHN'S DISEASE)的治療效果,有關營養狀况指標:總蛋白,白蛋白,鐵傳遞蛋白,前白蛋白和視黃醇結合蛋白與治療前比較,治療后均明顯升高。

有關炎症指標:白細胞數,紅細胞沉降率和C反應蛋白(CRP)與治療前比較,治療后均明顯減少。

根據炎症性腸病研究的國際組織(IOIBD)評分,51病例中,除一例外均有下降。 無任何病人有營養狀况惡化,51病例中有42例(82·4%)顯示最少中等度好轉。

有5例(8·1%)由于腹脹、腹痛和腹瀉等副作用而中斷治療,用這種低分子肽供應氮的 關道管飼處方,不但副作用少,并可改進營養狀況和減輕炎症進程。